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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/389,000	08/31/99	AFAR D	1703-018.US1

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EXAMINER	
DAVIS,M	
ART UNIT	**PAPER NUMBER**
1642	10

DATE MAILED: 02/14/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/389,000	Applicant(s) Afar et al
	Examiner Minh-Tam Davis	Group Art Unit 1642

☒ Responsive to communication(s) filed on *Jan 10, 2001*.

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-53* is/are pending in the application.

Of the above, claim(s) *5-12, 14-50, and 53* is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-4, 13, 51, and 52* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *1*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

Effective February 7, 1998, the Group Art Unit location has been changed, and the examiner of the application has been changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Minh-Tam Davis, Group Art Unit 1642.

Applicant's election with traverse of group I, claims 1-4, 13, 51 and 52 in Paper No. 9 is acknowledged. The traversal is on the ground(s) that separate searches would not be necessary to examine groups I-XVI, and it would not be a burden for the Examiner to examine all the claims together. This is not found persuasive because the searches for groups I-XVI are not co-extensive, and it would be a burden for the Examiner to examine all the claims together.

The requirement is still deemed proper and is therefore made FINAL.

Accordingly, claims 1-4, 13, 51 and 52 are examined in the instant application.

SEQUENCE RULE COMPLIANCE

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 C.F.R. 1.821-25 for the following reasons:

The sequences in figures 2, 3 are not accompanied by sequence identification numbers.

REJECTION UNDER 35 USC 112, SECOND PARAGRAPH

Claim 13 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 13 is indefinite, because claim 13 is dependent on non-elected claim 12.

DEPOSIT REQUIREMENT

The specification is objected to under 35 USC 112, first paragraph, as failing to provide an enabling disclosure and failing to provide an adequate description of the claimed invention without evidence that the claimed biological materials are known and readily available to the public or complete evidence of the deposit of the biological materials.

Although claim 5, to which the pending claim 13 is dependent, provides the name and accession number of the plasmid containing a polynucleotide encoding the claimed Phelix protein, the specification fails to provide an adequate description of the claimed invention, e.g. the name and address of the depositor, where the plasmid is deposited, and the date of the deposition. Moreover, applicant is required to submit an affidavit or declaration stating that all restrictions upon public access to the deposits will be irrevocably removed upon the granting of a patent on this application

The identifying information set forth in 37 CFR 1.809(d) should be added to the specification. See 37 CFR 1.803-1.809 for additional explanation of these requirements.

Claims 13 is rejected under USC 112, first paragraph, for the reasons set forth in the objection to the specification.

REJECTION UNDER 35 USC 101, UTILITY

35 U.S.C. § 101 reads as follows:

> "Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title".

Claims 1-4, 13, 51 and 52 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific asserted utility or a well established utility.

The specification discloses a polypeptide of SEQ ID NO:2 (PHELIX protein), which is deduced from an isolated cDNA sequence of SEQ ID NO:1. The disclosed utilities for the Phelix protein are diagnosis and treatment of cancer, using antibodies to the Phelix protein (p.16-17, 23-25). The specification however only discloses detection of Phelix mRNA (Figures 4-7). It is well known in the art that a gene could be regulated at different levels, transcriptional, translational and postranslational regulation (Shantz, LM et al, 1999, Internatl J Biochem & Cell Biol, 31: 107-122, especially p. 108, second column) and that not all mRNAs express as proteins. For example, there is no correlation between the level of p53 mRNA and the level of expression of p53 protein in blast cells from patients with acute myelogenous leukemia (Fu, L et al, 1996, Embo J, 15(16): 4392-4401, see abstract). Thus, it is not clear whether the claimed polypeptide of SEQ ID NO:2 even exists in nature. Thus, although the specification discloses that Phelix mRNA is expressed at high levels in various human cancers, and is not found in various normal tissues, except in normal testis, the utility for the Phelix protein is not credible, because the

actual overexpression of Phelix as protein in cancer tissues is questionable. The specification essentially gives an invitation to experiment wherein the artisan is invited to elaborate a functional use for the disclosed polypeptide.

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, WRITTEN DESCRIPTION

The instant specification does not contain a written description of the invention in such full, clear, concise, and exact terms or in sufficient detail that one skilléd in the art can reasonably conclude that applicant had possession of the claimed invention at the time of filing.

1. The claims 1-4 are drawn to 1) a polypeptide of SEQ ID NO:2 (PHELIX protein), 2) a polypeptide of at least 15 contiguous amino acids of SEQ ID NO:2, or a polypeptide of at least 15 contiguous amino acids of a polypeptide, which is at least 90% identical to SEQ ID NO:2 over its entire length.

The specification discloses a polypeptide of SEQ ID NO:2 (PHELIX protein), which is deduced from an isolated cDNA sequence of SEQ ID NO:1. The claims, as written, however, encompass polypeptides encoded by polynucleotides which vary substantially in length and also in nucleotide composition. The broadly claimed genus encompasses the Phelix protein of SEQ ID NO:2 encoded by the Phelix gene of SEQ ID NO:1, as well as polypeptides encoded by genes incorporating only portions of the disclosed sequence.

Although drawn specifically to the DNA art, the findings of *The Regents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412) are clearly relevant to the instant rejection. The court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every

species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention". The specification discloses only a single common structural feature, i.e. SEQ ID NO:2, a fragment of at least 15 contiguous amino acids which are shared by members of the claimed genus. Since the claimed genus encompasses polypetides encoded by genes yet to be discovered, the disclosed structural feature does not constitute the claimed genus. The instant specification fails to provide sufficient descriptive information, such as definitive strutural or functional features of the claimed genus of polynucleotides. There is no description of the conserved regions which are critical to the structure and function of the genus claimed. There is no description, however, of the sites at which variability may be tolerated and there is no information regarding the relation of structure to function. Structural freatures that could distinguish the compounds in the genus from others excluded are missing from the disclosure. Furthermore, the prior art does not provide compensatory structural or correlative teachings sufficient to enable one of skill to isolate and identify the polyppetides encoded by the polynucleotides encompassed and no identifying characteristic or property of the instant polynucleotides is provided such that one of skill would be able to predictably identify the encompassed molecules as being identical to those instantly claimed. Therefore, the disclosure of a polypeptide of SEQ ID NO:2 does not provide an adequate description of the claimed genus. Only a polypeptide of SEQ ID NO:2, encoded by SEQ ID NO: 1, but not the full breadth of the claims meet the written description provisions of 35 USC 112, first paragraph.

One of skill in the art would reasonably conclude that applicant was not in possession of the genus polypeptides having at least 15 contiguous amino acids of SEQ ID NO:2, or a polypeptide of at least 15 contiguous amino acids of a polypeptide, which is at least 90% identical to SEQ ID NO:2 over its entire length.

2. Claims 1 and 3 are drawn to a polypeptide, which is at least 90% identical to SEQ ID NO:2 over its entire length.

Claims 1 and 3 read on allelic variants and homologs of SEQ ID NO:2.

Reiger et al (Glossary of Genetics and Cytogenetics, Classical and Molecular, 4th Ed., Springer-Verlay, Berlin, 1976) clearly define alleles as one of two or more alternative forms of a gene occupying the same locus on a particular chromosome..... and differing from other alleles of that locus at one or more mutational sites (page 17). Thus, the structure of naturally occurring allelic sequences are not defined. The above case law applies as well to the instant polypeptide allelic variant rejection. With the exception of SEQ ID NO:2, the skilled artisan cannot envision the detailed structure of the polypeptides encoded by the encompassed polynucleotides and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. The nucleic acid itself is required. See *Fiers v. Revel*, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Lts.*, 18 USPQ2d 1016.

Further, although drawn specifically to the DNA art, the findings of *The Regents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412) are clearly relevant to the instant polypeptide variant rejection. The court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are

not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention".

The specification discloses that the invention includes allelic variants, conservative substitution variants and homologs of the Phelix protein (p.14). The specification discloses that conservative amino acid substitution can be made throughout the peptide encoded by the claimed nucleotide sequences (p.14). No further description of variants by substitution is provided in the specification.

The claim however reads on variants of SEQ ID NO:2, wherein said variants have any type of deletion, addition, or substitution besides conservative substitution, at any amino acid, throughout the length of the peptide. The specification and the claim do not place any limit on which amino acid to be subjected to non-conservative substitution, the type of substitution besides conservative substitution, nor the type of amino acids replacing the original amino acids. In addition, the specification and the claim do not place any limit on the number of amino acids that could be substituted. Thus the scope of the claim includes nucleotide sequences encoding numerous structural variants. Although the specification discloses that the types of changes are routinely done in the art, the specification and the claim do not provide any guidance as to which, or how many original amino acid(s) to be substituted, or to which type of substitution besides conservative substitution. Structural features, that could distinguish the claimed variants from the polypeptides known in the art, are missing from the disclosure. No common structural attributes that identify the claimed variants are disclosed. In addition, no common functional attributes that identify the claimed variants are disclosed, because the function

of a polypeptide sequence could be abolished, even with substitution of only one amino acid (Burgess et al. Journal of Cell Biology, 1990, 11: 2129-2138). The general knowledge and level of skill in the art do not supplement the omitted description, because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the claimed variants, SEQ ID NO:2 alone is insufficient to describe the claimed variants. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of polypeptide variants. Thus, applicant was not in possession of the claimed variants.

Thus, there is insufficient support of claims 1 and 3 as provided by the Interim Written Description Guidelines published in the June 5, 1998 Federal Register at Volume 63, Number 114, pages 32639-32645. Therefore, only an isolated polypeptide consisting of SEQ ID NO:2, but not the full breadth of the claims meets the written description provision of 35 USC 112, first paragraph.

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, ENABLEMENT

The following is a quotation of the first paragraph of 35 U.S.C. 112:

"The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention."

1. Claims 1-4, 13, 51 and 52 are rejected under 35 U.S.C. 112, first paragraph.

Specifically, since the claimed invention is not supported by a well established utility, and a clear written description for the reasons set forth in the rejection under 35

USC 101, and 112, first paragraph above, one skilled in the art clearly would not know how to use the claimed invention.

2. Claims 1, 2, 51 and 52 are rejected under 35 U.S.C. 112, first paragraph.

Claims 1, 2, 51 and 52 are drawn to a vaccine composition for the treatment of cancer, comprising a Phelix protein of SEQ ID NO:2 or an immunogenic portion of the Phelix protein.

It is questionable that the claimed Phelix protein or an immunogenic portion of the Phelix protein could be used as vaccine for treating cancer, because the specification only discloses detection of Phelix mRNA in cancer cells, and it is not even known whether cancer cells actually overexpress Phelix protein.

Even if cancer cells overexpress Phelix protein, one cannot extrapolate the teaching of the specification to the claims because it is well known that the art of anticancer drug discovery for cancer therapy is highly unpredictable, for example, Gura (Science, 1997, 278:1041-1042) teaches that researchers face the problem of sifting through potential anticancer agents to find ones promising enough to make human clinical trials worthwhile and teach that since formal screening began in 1955, many thousands of drugs have shown activity in either cell or animal models but that only 39 have actually been shown to be useful for chemotherapy (p. 1041, see first and second para). Because of the known unpredictability of the art, in the absence of experimental evidence, no one skilled in the art would accept the assertion that the claimed Phelix polypeptide or immunogenic portion thereof would be effective in treating cancer. Further, the refractory nature of cancer to drugs is well known in the art. Jain (Sci. Am., 1994, 271:58-65) teaches that tumors resist penetration by drugs (p.58, col 1) and that scientists need to put expanded effort into uncovering the reasons why therapeutic agents that show encouraging promise in the laboratory often turn out to be ineffective in the treatment of common solid tumors (p. 65, col 3). Curti (Crit. Rev. in Oncology/Hematology, 1993,

14:29-39) teaches that solid tumors resist destruction by chemotherapy agents and that although strategies to overcome defense mechanisms of neoplastic cells have been developed and tested in a number of patients, success has been limited and further teaches that it is certainly possible that cancer cells possess many as yet undefined additional molecular mechanisms to defeat chemotherapy treatment strategies and if this is true, designing effective chemotherapeutic regimens for solid tumors may prove a daunting task (para bridging pages 29-30) and concludes that knowledge about the physical barriers to drug delivery in tumors is a work in progress (p. 36, col 2). It is clear that based on the state of the art, in the absence of experimental evidence, no one skilled in the art would accept the assertion that the claimed Phelix polypeptide or immunogenic portion thereof would be effective in treating cancer. In addition, Hartwell et al (Science, 1997, 278:1064-1068) teach that an effective chemotherapeutic must selectively kill tumor cells, that most anticancer drugs have been discovered by serendipity and that the molecular alterations that provide selective tumor cell killing are unknown and that even understanding the detailed molecular mechanism by which a drug acts often provides little insight into why the treated tumor cell dies (para bridging pages 1064-1065) and Jain (cited supra) specifically teaches that systemic treatment typically consists of chemotherapeutic drugs that are toxic to dividing cells (p. 58, col 2, para 2). In addition, anti-tumor agents and those that prevent, reduce, retard or eliminate secretion of metastatic promoters, must accomplish several tasks to be effective. They must be delivered into the circulation that supplies the tumor or metastatic promotor producing cells and interact at the proper site of action and must do so at a sufficient concentration and for a sufficient period of time. It is clear, as disclosed above that the specification does not teach how to make/use a formulation with a targeting molecule. Also, the target cell must not have an alternate means of survival despite action at the proper site for the drug. In addition variables such as biological stability, half-life or clearance from the blood are important parameters in

achieving successful therapy. The formulation may be inactivated *in vivo* before producing a sufficient effect, for example, by degradation, immunological activation or due to an inherently short half life of the formulation. In addition, the formulation may not otherwise reach the target because of its inability to penetrate tissues or cells where its activity is to be exerted, may be absorbed by fluids, cells and tissues where the formulation has no effect, circulation into the target area may be insufficient to carry the formulation and a large enough local concentration may not be established. The specification provides insufficient guidance with regard to the issues raised above and provides no working examples which would provide guidance to one skilled in the art and no evidence has been provided which would allow one of skill in the art to predict the efficacy of the claimed Phelix protein in treating cancer with a reasonable expectation of success. In view of the above, one of skill in the art would be forced into undue experimentation to practice the claimed invention.

Further, the specification provides no exemplification of or guidance on how to use the claimed vaccine formulation or antigen for active immunotherapy in humans. The goal of tumor vaccination is the induction of tumor immunity to prevent tumor recurrence and to eliminate residual disease. However, Ezzell (J. NIH Res, 1995, 7:46-49) reviews the current thinking in cancer vaccines and states that tumor immunologists are reluctant to place bets on which cancer vaccine approach will prove effective in the long run (see the entire document, particularly last paragraph) and further states that no one is very optimistic that a single peptide will trigger an immune response strong enough to eradicate tumors or even to prevent the later growth of micrometastases among patients whose tumors have been surgically removed or killed by radiation or chemotherapy (p 48, para 6). In addition, Spitler (Cancer Biotherapy, 1995, 10:1-3) recognizes the lack of predictability of the nature of the art when she states that "Ask practicing oncologists what they think about cancer vaccines and you're likely to get the following response: "cancer

vaccines don't work". Ask a venture capitalist or the director of product development at a large pharmaceutical company and you're likely to get the same response." (p 1, para 1).

Furthermore, Boon (Adv Can Res, 1992, 58:177-210) teaches that for active immunization in human patients we have to stimulate immune defenses of organisms that have often carried a large tumor burden. Establishment of immune tolerance may therefore have occurred and it may prevent immunization and several lines of evidence suggest that large tumor burdens can tolerize or at least depress the capability to respond against the tumor (p. 206, para 2). In addition, Boon teaches even if activated CTLs are significantly increased, the therapeutic success remains unpredictable due to inconsistencies in antigen expression or presentation by tumor cells (p.178, paragraph before last paragraph). In view of the above, one of skill in the art would be forced into undue experimentation to practice the claimed invention.

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, SCOPE

In the event that Applicant could overcome the above 101, and 112, first paragraph rejections, claims 1, 3 and 4 still rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a Phelix protein of SEQ ID NO:2, does not reasonably provide enablement for a polypeptide, which is at least 90% identical to SEQ ID NO:2 over its entire length, and a polypeptide of at least 15 contiguous amino acids of a polypeptide, which is at least 90% identical to SEQ ID NO:2 over its entire length. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 1, 3 and 4 are drawn to a polypeptide, which is at least 90% identical to SEQ ID NO:2 over its entire length, and a polypeptide of at least 15 contiguous amino acids of a polypeptide, which is at least 90% identical to SEQ ID NO:2 over its entire

length. Claims 1, 3 and 4 read on variants of SEQ ID NO:2, and a polypeptide of at least 15 contiguous amino acids of said variants.

Applicants have not shown that the claimed variants are capable of functioning as that which is being disclosed.

It is pointed out that the term "variant" encompasses a variety of definitions, i.e. chemical modification, deletions, truncations, substitutions, conjugation, etc.. Applicants have not enabled these types of modified proteins in the specification.

Protein chemistry is probably one of the most unpredictable areas of biotechnology. For example, replacement of a single lysine residue at position 118 of acidic fibroblast growth factor by glutamic acid led to the substantial loss of heparin binding, receptor binding and biological activity of the protein (Burgess et al. Journal of Cell Biology, 1990, 11: 2129-2138). In transforming growth factor alpha, replacement of aspartic acid at position 47 with alanine or asparagine did not affect biological activity while replacement with serine or glutamic acid sharply reduced the biological activity of the mitogen (Lazar et al. Molecular and Cell Biology, 1988, 8: 1247-1252). Similarly, it has been shown that aglycosylation of antibodies reduces the resistance of the antibodies to proteolytic degradation, while CH2 deletions increase the binding affinity of the antibodies (see Tao. et al. The Journal of Immunology, 1989, 143(8): 2595-2601, and Gillies et al. Human Antibodies and Hybridomas, 1990, 1(1): 47-54). These references demonstrate that even a single amino acid substitution or what appears to be an inconsequential chemical modification will often dramatically affect the biological activity and characteristic of a protein.

In view of the above unpredictability, one of skill in the art would be forced into undue experimentation in order to perform the claimed invention as broadly as claimed

REJECTION UNDER 35 USC 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

1. Claims 2 and 4 are rejected under 35 U.S.C. 102(a or b) as being anticipated by Hillier et al , Genbank Sequence Database (Accession No: AA293855), National Center for Biotechnology Information, National Library of Medicine, Bethesda, Maryland, publicly available on 1997.

Claims 2 and 4 are drawn to a polypeptide of at least 15 contiguous amino acids of the protein of SEQ ID NO:2, and a polypeptide of at least 15 contiguous amino acids of a polypeptide, which is at least 90% identical to the protein of SEQ ID NO:2 over its entire length.

Hillier et al, 1997, teach a polynucleotide sequence which is 99% similar to the claimed SEQ ID NO:1, from nucleotide 13 to 503, under MPSRCH sequence similarity search (us-09-389-000-1.rst, p.4).

Given the polynucleotide sequence taught by Hillier et al, 1997, one of ordinary skill in the art would immediately envision the claimed polypeptide.

2. Claims 2 and 4 are rejected under 35 U.S.C. 102(b) as being anticipated by Hillier et al, Genbank Sequence Database (Accession No: R13043), National Center for Biotechnology Information, National Library of Medicine, Bethesda, Maryland, publicly available on 1995.

Claims 2 and 4 are drawn to a polypeptide of at least 15 contiguous amino acids of the protein of SEQ ID NO:2, and a polypeptide of at least 15 contiguous amino acids of a polypeptide, which is at least 90% identical to the protein of SEQ ID NO:2 over its entire length.

Hillier et al, 1995, teach a polynucleotide sequence which is 96% similar to the claimed SEQ ID NO:1, from nucleotide 891 to 1306, under MPSRCH sequence similarity search (us-09-389-000-1.rst, p.5).

Given the polynucleotide sequence taught by Hillier et al, 1995, one of ordinary skill in the art would immediately envision the claimed polypeptide.

REJECTION UNDER 35 USC 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 2 and 52 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hillier et al, 1995, 1997, *supra*, in view of Johnstone and Thorpe (Immunochemistry in Practice, 2nd Ed., 1987, Blackwell Scientific Publications, Oxford, pages 49-50).

Claims 2 and 52 are drawn to a vaccine composition comprising an immunogenic portion of at least 15 contiguous amino acid of a protein of SEQ ID NO:2 and a physiologically acceptable carrier.

Claim 52 recites the claimed immunogenic portion, formulated as a vaccine for treating cancer. However, this limitation is viewed as a recitation of intended use and therefore is not given patentable weight in comparing the claims with the prior art. Claims read on the ingredient per se, which is an immunogenic portion of at least 15 contiguous amino acid of a protein of SEQ ID NO:2.

The teaching of Hillier et al, 1995, 1997, has been set forth.

Hillier et al do not teach a physiologically acceptable carrier.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to include a carrier in the composition because Johnstone and Thorpe teach that it was common practice in the art at the time of applicant's invention to formulate compositions of antibodies and PBS, which is considered to be an acceptable carrier for storage of antibodies, i.e. proteins, p. 49 and 50. One of ordinary skill would have been motivated to do so in order to develop compositions suitable for storage. Finally, it has been held by the Court that a compound and a carrier are obvious, if it is obvious in the art to utilize a carrier with related compounds. See *In re Rosicky*, 125 USPQ 341 (CCPA 1960).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Minh-Tam B. Davis whose telephone number is (703) 305-

2008. The examiner can normally be reached on Monday-Friday from 9:30am to 3:30pm, except on Wesnesday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Tony Caputa, can be reached on (703) 308-3995. The fax phone number for this Group is (703) 308-4227.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0916.

Minh-Tam B. Davis

January 21, 2001